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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,915	11/28/2000	Naoki Nakayama	99,569-A	8656

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EXAMINER

ROMEO, DAVID S

ART UNIT PAPER NUMBER

1647

DATE MAILED: 06/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/724,915

Applicant(s)

NAKAYAMA ET AL.

Examiner

David S Romeo

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 10, 11, 45 and 57 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1 is/are allowed.
- 6) ☒ Claim(s) 2-8, 10, 11, 45 and 57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 57 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 0903.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

The amendment filed 09/25/2003 has been entered. Claims 1-8, 10, 11, 45, 57 are pending.

5 Applicant's election without traverse of the species of nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 8, wherein the Met residue at position 4 may be substituted with an Ile residue in Paper No./the paper filed 03/05/2004 is acknowledged.

10 Claim 57 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) to the extent that it is drawn to a non-elected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No./the paper filed 03/05/2004.

Maintained Formal Matters, Objections, and/or Rejections:

15 Claims 2-8, 10, 11, 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

20 The rejection of record is applied to claim 57.

Applicants argue that one of ordinary skill in the art would readily recognize the specific activities possessed by CHL polypeptides, including CHL binding to and antagonizing BMP-4,

Art Unit: 1647

and, therefore, the claims are not directed to a genus of nucleic acid molecules defined only by some level of nucleotide similarity. Applicant's arguments have been fully considered but they are not persuasive. In the absence of a limitation to a particular activity the claims are broadly and reasonably interpreted to encompass any and/or all activities, whether disclosed or not. In this absence, it is impossible to ascertain the limitations imposed by "an activity." Therefore, the examiner concludes that the claims are directed to a genus of nucleic acid molecules defined only by some level of nucleotide or amino acid sequence similarity. To argue that the claims must include a limitation found in the specification is improper.

Applicants argue that the genus of molecules encompassed by claim 2 is not highly variant, that the number of nucleotide substitutions is limited by the requirement that the polypeptide have an activity of the polypeptide of SEQ ID NO: 8, that one of ordinary skill in the art would readily recognize the specific activities possessed by CHL polypeptides, and that one of ordinary skill in the art could readily determine the structure of the nucleic acid molecules falling within the scope of the claims. Applicant's arguments have been fully considered but they are not persuasive. In the absence of a limitation to a particular activity the claims are broadly and reasonably interpreted to encompass any and/or all activities, whether disclosed or not. Thus, it is unclear how "an activity of the polypeptide set forth in SEQ ID NO: 8" limits the structure of the claimed polynucleotide. The limitation "wherein the residue ... -lysine" is ambiguous, as discussed below, and in one sense does not limit the structure of the claimed polynucleotide at all. Thus the claims do not require that any particular conserved or non-conserved portion be substituted or remain intact.

Applicants argue that that the genus of molecules encompassed by claim 3 is not highly variant, that the number of amino acid substitutions is limited by the requirement that the polypeptide have an activity of the polypeptide of SEQ ID NO: 8, that one of ordinary skill in the art would readily recognize the specific activities possessed by CHL polypeptides, that the application teaches the amino acid sequences of murine, rat, human CHL-like polypeptides. Applicant's arguments have been fully considered but they are not persuasive. In the absence of a limitation to a particular activity the claims are broadly and reasonably interpreted to encompass any and/or all activities, whether disclosed or not. Thus, it is unclear how "an activity of the polypeptide set forth in SEQ ID NO: 8" limits the structure of the claimed polynucleotide. Although claim 3(a) is limited to conservative amino acid substitutions, the claims place no limit on the number of substitutions and do not require that any particular conserved or non-conserved portion be substituted or remain intact. Furthermore, a single amino acid of SEQ ID NO: 8 is "a polypeptide as set forth in SEQ ID NO: 8 having a C- and/or N-terminal truncation." The limitation "comprises at least 377 amino acid residues" does not limit the encoded polypeptide to at least 377 amino acid residues of SEQ ID NO: 8. Thus, the structure of the encoded polypeptide encompasses polypeptides at least 377 amino acids long and comprising a single amino acid of SEQ ID NO: 8. Therefore, the genus of molecules encompassed by claim 3 is highly variant.

Claims 2-8, 10, 11, 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 8, does not reasonably provide enablement for claims 2a, 3a, 3b, or 3c.

Art Unit: 1647

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The rejection of record is applied to claim 57.

5 Applicants argue that the specification's teachings combined with what is well known in the art would enable one of ordinary skill in the art to make and use the full scope of the claimed invention without undue experimentation. Applicant's arguments have been fully considered but they are not persuasive. In the absence of a limitation to a particular activity the claims are broadly and reasonably interpreted to encompass any and/or all activities, whether disclosed or
10 not. Thus, it is unclear how "an activity of the polypeptide set forth in SEQ ID NO: 8" limits the structure of the claimed polynucleotide. Furthermore, a single amino acid of SEQ ID NO: 8 is "a polypeptide as set forth in SEQ ID NO: 8 having a C- and/or N-terminal truncation." The limitation "comprises at least 377 amino acid residues" does not limit the encoded polypeptide to at least 377 amino acid residues of SEQ ID NO: 8. Thus, the structure of the encoded
15 polypeptide encompasses polypeptides at least 377 amino acids long and comprising a single amino acid of SEQ ID NO: 8. Reciting "an activity of the polypeptide set forth in SEQ ID NO: 8" is not a disclosure of how to make and use the claimed polynucleotide because the specification lacks guidance for the amino acids in SEQ ID NO: 8 that are essential for "an activity" and those that are either expendable or substitutable. In the absence of this information
20 a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional random mutation analysis before they could even begin to rationally design a functional polypeptide having "an activity" other than a natural

Art Unit: 1647

amino acid sequence. Unless one has a reasonable expectation that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are more likely to work than not without actually making and testing them
5 then the instant application does not support the breadth of the claims.

Claims 2-8, 10, 11, 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are indefinite over the recitation of "an activity"
10 of the polypeptide set forth in SEQ ID NO: 8.

Applicants argue that the specification teaches several specific activities possessed by CHL polypeptides, and that one of ordinary skill in the art would understand the meaning of the phrase. Applicant's arguments have been fully considered but they are not persuasive. The specification teaches that CHL related polypeptides possess at least one activity of the
15 polypeptide as set forth in SEQ ID NO: 8 (page 15, lines 12-15). The specification also describes methods of assaying for modulators of CHL polypeptide activity without pointing to one particular activity of a CHL polypeptide. In the absence of a limitation to a particular activity the claims are broadly and reasonably interpreted to encompass any and/or all activities, whether disclosed or not. It is unclear what activity is intended and how to ascertain the metes
20 and bounds of the claimed invention. The metes and bounds are not clearly set forth.

Claim Rejections - 35 USC § 102

Claims 3-5, 7, 11, 45 are rejected under 35 U.S.C. 102(a) as being anticipated by Jacobs (10, cited by Applicants).

Applicants argue that Jacobs does not disclose a nucleic acid molecule encoding a polypeptide fragment of SEQ ID NO: 8 of at least 377 amino acid residues. Applicant's arguments have been fully considered but they are not persuasive. Claim 3c is ambiguous, as discussed below. Therefore, the claims do not recite a 377 amino acid fragment of SEQ ID NO: 8. Furthermore, any single amino acid residue of SEQ ID NO: 8 is "SEQ ID NO: 8 having a C- and/or N-terminal truncation." Jacobs discloses an isolated nucleic acid molecule wherein the isolated nucleic acid molecule comprises a nucleotide sequence encoding at least a 377 amino acid polypeptide wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 8 having a C- and/or N-terminal truncation.

New Formal Matters, Objections, and/or Rejections:

Claim Objections

Claims 8 and 10 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

Claims 2-8, 10, 11, 45, 57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

Art Unit: 1647

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Support for the following particular limitations cannot be found in the disclosure as originally filed and their introduction raises the issue of new matter: “377 amino acid residues,” “1131 nucleotides,” “wherein the residue at position 95 ... -lysine,” and the species and/or subgenera of amino acid substitutions in claim 57. In addition, support for the combination of these particular limitations with the other limitations in claims 2a, 3b, 3c, and 57 cannot be found in the disclosure as originally filed and raises the issue of new matter.

10 Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 recites the limitation "the percent identity" in line 2. There is insufficient antecedent basis for this limitation in the claim.

15 Claims 2, 4-8, 10, 11, 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are indefinite over the recitation of “wherein the residue at position 95 ... and the residues at positions 319-323” because it is unclear if the residue at position 95 of SEQ ID NO: 8 and the residues at positions 319-323 of SEQ ID NO: 8
20 are intended or if the residue at position 95 of the encoded polypeptide and the residues at positions 319-323 of the encoded polypeptide are intended. The metes and bounds are not clearly set forth.

Claims 3-8, 10, 11, 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5 The claims are indefinite over the recitation of “an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 having a C- and/or N-terminal truncation, wherein the encoded polypeptide comprises at least 377 amino acid residues” (claim 3(b)) and over the recitation of “an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 8 with at
10 least one modification that is a conservative amino acid substitution, C-terminal truncation, or N-terminal truncation, wherein the encoded polypeptide ... comprises at least 377 amino acid residues” (claim 3(c)).

In the case of the former it is unclear if:

15 the isolated nucleic acid molecule comprises a nucleotide sequence encoding a polypeptide comprising at least 377 amino acid residues of SEQ ID NO: 8; or

 the isolated nucleic acid molecule comprises a nucleotide sequence encoding at least a 377 amino acid polypeptide wherein the polypeptide comprises the amino acid sequence of SEQ ID NO: 8 having a C- and/or N-terminal truncation.

In the case of the latter it is unclear if:

20 the isolated nucleic acid molecule comprises a nucleotide sequence encoding a polypeptide comprising at least 377 amino acid residues of SEQ ID NO: 8, wherein the

Art Unit: 1647

remaining amino acid residues in SEQ ID NO: 8 can have at least one modification that is a conservative amino acid substitution, C-terminal truncation, or N-terminal truncation; or

the isolated nucleic acid molecule comprises a nucleotide sequence encoding at least a 377 amino acid polypeptide wherein the polypeptide comprises the amino acid sequence of SEQ

5 ID NO: 8 with at least one modification that is a conservative amino acid substitution, C-terminal truncation, or N-terminal truncation.

The meaning of these alternative embodiments is different. Therefore, the claim is ambiguous. The metes and bounds are not clearly set forth.

10 Claims 2-8, 10, 11, 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are indefinite because “comprising a nucleotide sequence (b) a region of the nucleotide sequence,” “comprising a nucleotide sequence (c) a region of the nucleotide sequence,” “comprising a nucleotide sequence (d) a nucleotide
15 sequence,” and “comprising a nucleotide sequence (d) the nucleotide sequence,” don’t make any sense. The metes and bounds are not clearly set forth.

Claim Rejections - 35 USC § 102

Claims 3-8, 10, 45 are rejected under 35 U.S.C. 102(b) as being anticipated by De
20 Robertis (A).

The claims are directed to or encompass an isolated nucleic acid molecule comprising a nucleotide sequence encoding at least a 377 amino acid polypeptide wherein the polypeptide

Art Unit: 1647

comprises the amino acid sequence of SEQ ID NO: 8 having a C- and/or N-terminal truncation, wherein "SEQ ID NO: 8 having a C- and/or N-terminal truncation" encompasses a single amino acid of SEQ ID NO: 8.

DeRobertis discloses an isolated nucleic acid molecule encoding a polypeptide
5 comprising at least 377 amino acid residues and at least a single amino acid of SEQ ID NO: 8 (paragraph bridging columns 4-5; column 5, lines 30-35; column 6, full paragraph 3) operatively linked to expression control sequences other than the native CHL gene promoter, viral expression vectors comprising same, bacterial and eukaryotic host cells comprising the expression vectors, and a method of producing the encoded polypeptide (column 7, line 17,
10 through column 8, line 50).

Conclusion

Claim 1 is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this
15 Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after
20 the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

Art Unit: 1647

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (571) 272-0887.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306

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CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.



DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
JUNE 2, 2004